Amendments to the Specification:

Please replace the paragraph under the title on page 1 with the following amended paragraph:

> This application is a division of application Serial No. 09/390,326, filed September 7, 1999, now U.S. Patent No. 6,316,603, which ~~is based upon~~ claims the benefit of Provisional application Serial No. 60/099,503, filed September 8, 1998.

On page 2, please replace the first paragraph under the heading, "Background of the Invention," with the following amended paragraph. **Please note** that underlining present in the original text has been changed to italics in the following replacement paragraph, to make presentation of changes more readable.

> Many physiological events including embryogenesis, organ development, estrus, and wound healing require vascular growth and remodeling (Folkman et al., (1992) *J. Biol. Chem. 267*, 10931-10934; Risau, W. (1995) *FASEB J. 9*, 926-933.). In addition to these beneficial processes, angiogenesis is also involved in the proliferation of disease states such as tumor growth, metastasis, psoriasis, rheumatoid arthritis, macular degeneration and retinopathy (Pepper, M.S., (1996) *Vasc. Med. 1*, 259-266; Kuiper et al., (1998) *Pharmacol. Res. 37*, 1-16, 1998; Kumar and Fidler, (1998) *In Vivo 18*, 27-34; Szekanecz et al., (1998) *J. Investig. Med. 46*, 27-41; Tolentino and Adamis, (1988) *Int. Ophthalmol. Clin. 38*, 77-94. Of the signaling pathways known to influence vascular formation, these involving vascular endothelial growth factor (VEGF) haves been shown to be essential and selective for vascular endothelial cells (Dvorak et al., (1995) *Am. J. Path. 146*, 1029-1039; Thomas, K., (1996) ~~*Cell*~~ *J. Biol. Chem. 271*, 603-606; Ferrara N. and Davis-Smyth, (1997) *Endocrine Rev. 18,* 4-25). The therapeutic potential of inhibiting the VEGF pathway has been directly demonstrated by anti-VEGF monoclonal antibodies which were active against a variety of human tumors (Borgström et al, (1996) *Cancer Res. 56*, 4032-4039) and ischemic retinal disease (Adamis et al., (1996) *Arch. Ophthalmol. 114*, 66-71).

On page 8 of the substituted specification, before the heading, "Brief Description of the Drawings," please insert the following paragraph:

> In the following description, "VEGFR2Δ50" corresponds to SEQ ID NO: 5, and "PDGFRα" refers to SEQ ID No: 6.

On page 8 of the substituted specification, please replace the first paragraph after the heading, "Brief Description of the Drawings" with the following amended paragraph:

> Figure 1. Secondary structure assignments (as given by Procheck) for the catalytic domain of VEGFR2 and sequence alignment with other representative receptor tyrosine kinases. α helices are designated as αB-αI, β strands are designated as β1-β8. The site of 50 residue deletion in VEGFR2Δ50 is indicated by |. The site of the E990V mutation in ~~VEGFR2D50~~ VEGFR2Δ50 is denoted by an *. Sequences are from: VEGFR2 (SEQ ID No: 12) (reported here); FGFR1 (SEQ ID No: 7) (Swiss protein database #P11362); IRK (SEQ ID No: 8) (EMBL protein database #A18657; numbering as in Mohammadi et al., 1996); VEGFR1

(SEQ ID No: 9) (Swiss protein database #P17948); PDGFRα (SEQ ID No: 6) (Swiss protein database #P17948).

On page 9 of the substituted specification, please replace the paragraph under the subheading, "Cloning of the VEGFR-2 Protein," continuing on to page 10, with the following amended paragraph. **Please note** that underlining present in the original text has been changed to italics in the following replacement paragraph, to make presentation of changes more readable.

> The coding sequence (Terman et al., (1992) *Biochem Biophys. Res. Commun. 187*, 1579-86) for the cytoplasmic domain of the VEGFR-2 was amplified by PCR (Mullis et al., ~~(1986).~~ (1992) *Biotechnology 24*, 17-27) from a human aorta cDNA pool (Clontech Palo Alto, CA). Two overlapping sequences were amplified independently. Vcyt (residues M806-V1356), which represented the entire cytoplasmic domain, and Vcat (residues C817M-G1191), with boundaries based upon a primary amino acid sequence alignment with the insulin receptor kinase catalytic domain (Wei et al., (1995) *J. Biol. Chem. 270*, 8122-8130).

On page 11 of the substituted specification, please replace the third full paragraph, beginning with "Mutations were introduced," with the following replacement paragraph:

> Mutations were introduced by oligonucleotide site directed mutagenesis (Kunkel, 1985) using the Muta-Gene in vitro Mutagenesis Kit from (Bio-Rad Hercules, CA). The Vcat DNA fragment was subcloned from the pET24a vector using an NdeI-XhoI digest into the vector pMGH4 (Schoner et al., 1986, Kan et al., 1992) and this vector was used to generate the ssDNA uracil template (minus strand) in *E. coli* strain CJ236 supplied in the kit. An oligo (SEQ ID No: 10) (5'-CTCAGCAGGATTGATAAGACTACATTGTTC-3') was designed to create a construct (Vcat(ΔG1172-G1191)) which truncated the C-terminus to residue D1171. Another oligo (SEQ ID No: 11) (5'-GAATTTGTCCCCTACAAGGAAGCTCCTGAAGATCTG-3') was designed to delete the central 50 residues (residues T940-E989) of the insert kinase domain, based on a sequence alignment with FGFR1 (Mohammadi et al, 1996). Sequence analysis detected an inadvertent Glu990-Val mutation. All DNA modification and restriction enzymes were purchased from New England Biolabs and oligonucleotides were purchased form Genosys Biotechnology.